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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,601	04/03/2000	BERNARD ABRAMOVICI	IVD994	2604

5487 7590 11/16/2005

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,601	ABRAMOVICI ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-7 and 9-22 are pending in this application.

Response to Arguments

Applicant's arguments filed 24 June 2004 have been fully considered but they are not persuasive. The rejection made in the paper mailed 20 February 2004 is maintained and hereby repeated for the reasons set forth in the previous office action and those set forth below. It is the applicant's position that the cited references would not have suggested the applicants' invention because if the invention would have been obvious, the absorption problem related to amiodarone would have been solved long ago. Applicant's argument showing long felt need for a composition of amiodarone in a non-ionic hydrophilic surfactant is itself insufficient to outweigh the record of evidence of a *prima facie* case of obviousness, since failure to present any other objective evidence of non-obviousness rebuts the assertion that the composition actually satisfied long felt need within the industry. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Since the disclosure provided by the PDR recognizes the problem of solubility in amiodarone, the Story reference provides motivation for one to solubilize insoluble drugs using non-ionic

hydrophilic surfactants, and Margin-Algarra et al solve the absorption problem of amiodarone specifically by using the non-ionic hydrophilic surfactant, polysorbate 80, a *prima facie* case of obviousness is established.

Applicant argues that the proportion of surfactant to NSAID ratio is from 1:5.7 to 1:50. This fact is not germane to the case since the Story et al reference is used within the 35 U.S.C. §103(a) rejection to demonstrate that it is well-known that non-ionic surfactants such as polysorbate 80 are known and used in the art to solubilize insoluble drugs. As anyone of ordinary skill in the art will appreciate, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find *workable* conditions generally involves no more than the application of routine skill in the art of chemical engineering, as in altering the volume in which the dose of medication is to be administered. See, only as exemplary, the dicta of *In re Aller* 105 USPQ 233. Normally, change in temperature, concentration, or both, is not patentable modification; however, such changes may impart patentability to process if ranges claimed produce new and unexpected result which is different in kind and not merely in degree from results of prior art; such ranges are termed "critical" ranges, and applicant has burden of proving such criticality; even though applicant's modification results in great improvement and utility over prior art, it may still not be patentable if modification was within capabilities of one skilled in art; more particularly, where general conditions of claim are disclosed in prior art, it is not inventive to discover optimum or workable ranges by routine experimentation. Similarly, the determination of *optimal* values within a disclosed

range is generally considered obvious. See, only as exemplary, the dicta of *In re Boesch* 205 USPQ 215. Clearly, Martin-Algarra et al. recognize the problem of erratic and variable absorption of amiodarone and also recites that a small amount of non-ionic hydrophilic surfactant solves the problem. 7.5 mg of amiodarone is dissolved in 10 ml of 0.4mM of a polysorbate 80 solution. It is not clear to the examiner how applicant's representative arrived at a 700 fold greater amount of surfactant than in the instant invention. Martin-Algarra et al. teach the absorption rate constants of amiodarone *decreased* as the surfactant concentration *increased* and absorption was unusually fast at ***lower surfactant concentrations*** (see abstract).

The obvious type double patenting rejection made in the paper mailed 20 February 2004 is maintained and hereby repeated for the reasons set forth in the previous office action and those set forth below. Applicant asserts that there is nothing in the reference to suggest lyophilizing the mixture of active agent, buffer and surfactant to prepare a solid oral preparation nor is there anything suggest that oral administration of such a mixture would enhance the rate of absorption and reduce its variability. The examiner is in agreement that there is nothing to suggest lyophilizing the composition in the patent, however, the composition appears to be substantially the same, and to incorporate said liquid composition into a capsule capable of containing the liquid for oral administration would have been obvious.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Donna Jagoe
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Art Unit 1614

11/02/2005

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